REMARKS

In view of the above amendment and following remarks, the Examiner is requested to allow claims 1-36, the only claims pending and under examination in this application.

Formal Matters

Claim 1 has been amended to recite a preamble. Support for this amendment can be found in original Claim 1. As no new matter has been added by way of this amendment, entry thereof by the Examiner is respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-36 are rejected under 35 U.S.C. 1 12, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Specifically, the Examiner states that it is unclear what is meant by the terms "chromatographic conditions," "binding identity" and "pharmaceutical agent," and that it is therefore unclear what the scope of these claim limitations are in the context of the invention.

The Applicants respectfully submit that the cited terms are sufficiently clear to one of ordinary skill in the art, particularly in light of the instant specification.

With regard to the term "chromatographic conditions," the Applicants submit that chromatography and the conditions for performing such are exceptionally well known in the art, such that one of ordinary skill in the art readily understands that chromatographic conditions are those suitable to promote a desired specificity of binding obtainable by methods well known in the art. Additionally, the Applicants submit that the instant specification states at page 15, paragraph 50:

> Once a sample having at least one constituent is combined with a suitable mobile phase or binding buffer, the constituent-containing sample/mobile phase mixture is contacted

with one of the stationary phases of the subject invention under suitable conditions, e.g., suitable chromatographic conditions, to bind a fraction of the sample that includes at least one of the constituents present in the sample, i.e., to isolate the at least one constituent(s) from other constituents present in the sample. In this manner, one or more constituents are bound or otherwise retained for a period of time by this stationary phase while other constituents are passed through or over the stationary phase and eluted, e.g., for further analysis.

As such, both the claims and the specification make clear to one of ordinary skill in the art that chromatographic conditions are those suitable to bind a constituent of a sample and separate it from other constituents in a sample, the well-understood purpose of chromatography as known in the art.

With regard to the term "binding identity," the Applicants submit that, as discussed above, chromatography is exceptionally well known in the art such that in the context of the claims, one of ordinary skill in the art understands that binding identity is that characteristic of the constituent which is identified by contacting it with a stationary phase under chromatographic conditions. Additionally, the Applicants submit that the instant specification states at page 8, paragraph 30:

By "binding identity" is meant at least one aspect (e.g., a chemical aspect, physical aspect, biological activity aspect, and the like) of at least one binding partner member of a specific binding complex with respect to at least one binding assay. For example, such a binding identity may include the molecular structure of a molecule, e.g., the molecular structure of a protein component in a protein ligand binding interaction.

As such, both the claims and the specification make clear to one of ordinary skill in the art that binding identity is that characteristic of the constituent of a sample by which it is separated from the other constituents in a sample, which is the well-understood purpose of chromatography as known in the art and the clear purpose of the recited method.

With regard to the term "pharmaceutical agent," the Applicants submit that one of ordinary skill in the art readily understands that a pharmaceutical agent is an agent that is administered to treat a condition, i.e., a drug. The definition of

"pharmaceutical" as stated in the Merriam-Webster's Medical Dictionary (Merriam-Webster, Inc. 20 Sep. 2007. <Dictionary.com http://dictionary.reference.com/browse/pharmaceutical>) is as provided below:

> Main Entry: **pharmaceutical**
> Variant: *also* **pharmaceutic**
> Function: *noun*
> : a medicinal drug

Additionally, the Applicants submit that the instant specification states at page 21, paragraph 65:

> For example, in certain embodiments the subject invention may be employed to assess the binding specificity of a pharmaceutical agent, e.g., a pharmaceutical agent under development, for a particular protein. For example, a pharmaceutical agent may be intended to bind or be highly selective for a particular protein (i.e., an intended or target protein), but not others. Accordingly, the subject methods may be employed as a means to efficiently and effectively determine the binding identity, e.g., specificity, of a target protein for a particular pharmaceutical agent as well as to determine if the pharmaceutical agent binds other proteins as well.

The specification thereby makes clear to one of ordinary skill in the art that the claimed pharmaceutical agent may be a pharmaceutical agent under development, which is desired to have a particular binding specificity, which specificity is tested by the claimed method.

With regard to the scope of the cited phrases, the Applicants respectfully submit that the breadth of a claim is not to be equated with indefiniteness *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). In other words, simply because a wide range of, for example, pharmaceutical agents can be employed in the claimed methods, it does not mean that the term "pharmaceutical agent," as used in the instant claims, is indefinite. In the instant case, one of ordinary skill in the art would have no reason to conclude that the claimed method could not effectively be applied

to a very broad range of compounds or materials which might be of use as pharmaceutical agents if found to have a particular binding specificity.

Further, the art is replete with protocols teaching one of ordinary skill in the art how to arrive at chromatographic conditions suitable to promote a desired specificity of binding between a constituent of a sample and a stationary phase whose specificity for it is certain, as is claimed. Accordingly, the Applicants submit that the instant terms are clearly defined for the purposes of the claims, which claims are therefore definite.

In view of the foregoing discussion, it is believed that the rejection has been adequately addressed. Withdrawal of the rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 1-8, 14-21 and 27-36 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Bailey, Jerome *et al.* (hereinafter "Bailey," Removing High-Abundance Proteins from Serum, Genetic Engineering News, 1 November 2003, pp.32, 36-37, Vol. 23, No.19). The Applicants respectfully submit that all the limitations of the claims are not taught by the cited art.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

The instant claims are directed to, *inter alia*, a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of the second stationary phase for the at least one

constituent is certain, to at least determine the binding identity of the at least one constituent. It is not seen where this is taught by Bailey.

Bailey describes the use of a column with monoclonal antibodies fixed to a solid phase to remove known high-concentration proteins from serum. Bailey states that the Multiple Affinity Removal System was designed to "specifically and simultaneously remove six high-abundance proteins in human serum" (Bailey, page 32, second column). The Examiner alleges that Bailey teaches every element of the claims.

The Applicants respectfully submit that all of the monoclonal antibodies in the column described by Bailey are of known specificity to serum proteins, which serum proteins are listed in Figure 2 on page 32 of Bailey. All of the antibodies of Bailey are known and demonstrated to bind their targets with high specificity (Bailey, page 32, paragraph spanning columns 3-4, and throughout the reference). Accordingly, Bailey is silent regarding a first stationary phase in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, as claimed.

Further, the Applicants respectfully submit that Bailey specifically recites that the antibodies as used in the described system "simultaneously remove six high-abundance proteins." Accordingly, Bailey is further silent regarding sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, as claimed.

Accordingly, Bailey fails to teach at least these elements of the claims, and the rejection may be withdrawn.

Claims 1, 2, 6-16, 18, 20-27, 31 and 33-36 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Mizushina, YoshiYuki *et al.* (hereinafter "Mizushina," Flavonoid glycoside: A new inhibitor of eukaryotic DNA polymerase alpha and a new carrier for inhibitor-affinity chromatography, Biochemical and

Biophysical Research Communications, vol. 301, no. 2, pgs 480-487 (7 February 2003). The Applicants respectfully submit that all the limitations of the claims are not taught by the cited art.

The instant claims are directed to, *inter alia*, a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of the second stationary phase for the at least one constituent is certain, to at least determine the binding identity of the at least one constituent. It is not seen where this is taught by Mizushina.

The Examiner alleges that the concluding paragraph of Mizushina spanning pages 485-486, taken in combination with the left column of page 481, teaches that this method of Mizushina may be used to evaluate the specificity of a stationary phase comprising contacting a sample with at least a first stationary phase and second stationary phase under chromatographic conditions, wherein the specificity of said first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of said second stationary phase for said at least one constituent is certain.

The Applicants respectfully submit that the cited passages of Mizushina fail to teach what the Examiner alleges. The relevant passages of Mizushina, spanning pages 480-481, are reproduced below for convenience:

> Our original purpose was to use the newly found inhibitors as tools and molecular probes to distinguish DNA polymerases, and moreover, if possible, to clarify their biological and in vivo functions by using them. In the process, the most important thing at first was to collect and purify sufficient amounts of each of the polymerases for biochemical study. Even as of now, the precise properties of most of the eukaryotic polymerases remain unknown, because the molecular size of each of them is too large to produce them as recombinant proteins, and because most of them appear to be composed of catalytic and several other subunits. Therefore, they have been isolated directly from fresh tissues using many types of column chromatographies including antibody-conjugated columns. However, these methods are both

laborious and time-consuming. If the newly found inhibitors could be used in inhibitor-conjugated columns, the affinity chromatography would revolutionize the methodology used in the isolation of polymerases.

From this point of view, we tried to make inhibitor-columns using several inhibitors. Although the polymerases bound, they were not eluted from the columns, because the binding of the enzymes and the inhibitors was too tight. In this study, we report on newly found compounds that selectively inhibit the activities of eukaryotic replicative DNA polymerases. The two natural compounds are flavonoid glycosides, kaempferol 3-*O*-(6″-acetyl)-β-glucopyranoside (KAG) and quercetin 3-*O*-(6″-acetyl)-β-glucopyranoside (QAG), produced from a higher plant, a Japanese butterbur (*Petasites japonicus*). These compounds were originally isolated from the Norwegian spruce (*Picea abies* (L.) Karst., Pinaceae) in 1995, although the biochemical action mode was not reported [11]. The flavonoid glycosides could not only inhibit the DNA polymerase activities moderately, but also influenced several different species of polymerases. Subsequently, we synthesized a KAG-conjugated column and developed an inhibitor-affinity chromatography for eukaryotic DNA polymerases. The present results may provide a new approach in DNA polymerase inhibitor studies, in particular in eukaryotic DNA polymerase studies.

This is the extent of the teaching of Mizushina regarding the use of multiple inhibitors in a column. Applicants particularly note that Mizushina states that the technique of using multiple inhibitors in a column failed to work. As such, were one of ordinary skill in the art to consult Mizushina to learn how to identify DNA polymerase inhibitors, they would learn to use a single inhibitor in a column in order to be successful, as taught throughout the reference. Mizushina nowhere contradicts this teaching. In the concluding paragraph of Mizushina spanning pages 485-486, Mizushina states, "To isolate pol delta and epsilon, the KAG-column must be applicable. Whether or not the KAG- (or QAG-) column is also effective for isolating pol gamma, rho, theta and mu and the other polymerases found more recently is unknown as yet. However, if the inhibitors interact with some of them, it should also work." Accordingly, in going forward to identify an inhibitor which interacts with the other polymerase subtypes, Mizushina recommends using a single-inhibitor column such as a KAG- or QAG-column.

As such, the Applicants further respectfully point out that the cited passages and the entire disclosure of Mizushina fail to teach the claimed sequential contacting of the sample with at least a first stationary phase and a second stationary phase under chromatographic conditions. Mizushina merely describes attempting "to

make inhibitor-columns using several inhibitors." The Applicants submit that this description does not indicate any type of sequential contact to one of ordinary skill in the art, but instead indicates that the inhibitors are mixed together in no particular configuration, which mixing produces a technique that does not work.

Since Mizushina fails to teach sequential contacting, Mizushina further fails to teach the claimed sequential contacting in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of the second stationary phase for the at least one constituent is certain. Mizushina nowhere teaches any combination of inhibitors in a column one of which is known to bind polymerases and one of which is not known to bind, much less such inhibitors in any particular sequence.

Accordingly, Mizushina fails to teach at least these elements of the claims, and the rejection may be withdrawn.

Claims 1, 6-8, 14-16, 18, 20, 21, 27-31 and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Jindal et al. (hereinafter "Jindal," US Pub 2002/0150926). The Applicants respectfully submit that all the limitations of the claims are not taught by the cited art.

The instant claims are directed to, *inter alia*, a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase under chromatographic conditions, in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of the second stationary phase for the at least one constituent is certain, to at least determine the binding identity of the at least one constituent. It is not seen where this is taught by Jindal.

Jindal allegedly teaches multi-dimensional systems, for screening libraries to select, recover and characterize a candidate ligand with a desired or preselected

affinity K for a preselected target molecule (Jindal, paragraph 11). The method of Jindal allegedly can be used to screen candidate ligands for a ligand which will bind to a first target molecule but not to a second target molecule (Jindal, paragraph 119).

The Applicants respectfully point out that Jindal nowhere teaches that any of the ligands used has a specificity for a target which is certain. Indeed, since Jindal repeatedly makes clear throughout the reference that the described method is directed to screens for ligands, i.e., the discovery of compounds with one or several binding affinities which are unknown prior to the screen, the use of a ligand with a specificity for a target which is certain does not find use in the method of Jindal.

As such, Jindal fails to teach a method in which the specificity of the first stationary phase for at least one constituent present in the sample is at least uncertain, and the specificity of the second stationary phase for the at least one constituent is certain.

Since Jindal fails to teach the claimed stationary phase with a specificity for at least one constituent present in the sample which is certain, Jindal further fails to teach a method including sequentially contacting a sample with at least a first stationary phase and a second stationary phase, where the specificities are respectively uncertain and certain. Jindal nowhere teaches any combination of targets in a column one of which is known to bind a ligand and one of which is not known to bind, much less such targets in any particular sequence.

Accordingly, Jindal fails to teach at least these elements of the claims, and the rejection may be withdrawn.

CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at (650) 327-3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10030532-1.

Respectfully submitted,

Date: September 27, 2007

By: _____
Bret E. Field
Registration No. 37,620

AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599

F:\DOCUMENT\AGIL\125 (10030532-1)\10030532-1 Response to OA of 6-29-07.doc